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Prophylactic Warfarin Therapy After Primary Percutaneous Coronary Intervention for Anterior ST-Segment Elevation Myocardial Infarction

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ABSTRACT

OBJECTIVES This study sought to determine the benefits of adding oral anticoagulation therapy in patients with anterior wall ST-segment elevation myocardial infarction (STEMI) patients after primary percutaneous coronary intervention (PCI).

BACKGROUND Guidelines suggest adding oral anticoagulation to dual-antiplatelet therapy in patients with STEMI when left ventricular apical akinesis or dyskinesis is present to prevent thromboembolic complications. The benefits of this triple therapy remain unknown.

METHODS We identified patients with anterior STEMI referred (PCI) between July 2004 and June 2010 with apical akinesis or dyskinesis on transthoracic echocardiography. We compared patients who were prescribed warfarin to patients who were not. We excluded patients with left ventricular thrombus, a separate need for oral anticoagulation, and previous intracranial bleeding. The primary outcome was a composite of net adverse clinical events (NACE) consisting of all-cause mortality, stroke, reinfarction, and major bleeding at 180 days.

RESULTS Among 460 patients who qualified, 131 were discharged on warfarin therapy and 329 without warfarin therapy. Dual-antiplatelet therapy was prescribed for 99.2% of the patients in the warfarin group and for 97.6% of the patients in the no warfarin group ($p = 0.46$). Compared with patients in the no warfarin group, patients in the warfarin group had higher rates of NACE (14.7% vs. 4.6%, $p = 0.001$), death (5.4% vs. 1.5%, $p = 0.04$), stroke (3.1% vs. 0.3%, $p = 0.02$), and major bleeding (8.5% vs. 1.8%, $p < 0.0001$). By propensity score analysis, allocation to warfarin therapy was an independent predictor of NACE (odds ratio [OR]: 4.01, 95% confidence interval: 2.15 to 7.50, $p < 0.0001$). In a separate multivariable analysis, the OR of NACE remained significantly higher compared with patients who were not prescribed warfarin (OR: 3.13, 95% confidence interval: 1.34 to 7.22, $p = 0.007$).

CONCLUSIONS Our results do not support the addition of warfarin therapy after primary PCI in patients with apical akinesis or dyskinesis. (J Am Coll Cardiol Intv 2015;8:155–62) © 2015 by the American College of Cardiology Foundation.

Primary percutaneous coronary angioplasty (PCI) has become the dominant reperfusion strategy for ST-segment elevation myocardial infarction (STEMI) in many countries. In this setting, platelet inhibition is now recognized has key adjunctive therapy to prevent acute and long-term thrombotic complications after the intervention. Dual-antiplatelet therapy (DAPT) consisting of aspirin

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ABBREVIATIONS AND ACRONYMS

CI = confidence interval

DAPT = dual-antiplatelet therapy

INR = international normalized ratio

LV = left ventricular

NACE = net adverse clinical event(s)

OR = odds ratio

PCI = percutaneous coronary intervention

STEMI = ST-segment elevation myocardial infarction

TIMI = Thrombolysis In Myocardial Infarction

TTE = transthoracic echocardiography

and a $P2Y_{12}$ inhibitor reduces stent thrombosis and reinfarction after coronary stenting compared with aspirin alone or aspirin plus warfarin (1-4).

In some patients treated with primary PCI, there is need to add oral anticoagulants to prevent thromboembolic events. However, there is mounting evidence that the combination of DAPT and oral anticoagulation (triple therapy) is associated with bleeding (5-8). In the era of primary PCI, there are limited data on clinical outcomes in patients with STEMI who are prescribed triple therapy. The 2013 American College of Cardiology/American Heart Association STEMI guidelines recommend oral anticoagulation therapy with warfarin in addition to DAPT in patients with left ventricular (LV) mural thrombus (Class 2a recommendation) and in patients with apical akinesis or dyskinesis (class 2b recommendation) for at least 3 months (9).

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The transthoracic echocardiography (TTE) is the most widely used tool to assess for LV thrombus and wall motion abnormalities after anterior STEMI. Although there is consensus to add oral anticoagulants when LV thrombus is identified, the role of anticoagulants in patients with apical akinesis or dyskinesis without demonstrated LV thrombus remains controversial. Moreover, the safety of this approach in the latter group is poorly documented and represents a major therapeutic dilemma. As randomized trials have yet to be done, we used our database to provide insight into this important management question.

METHODS

PATIENT SELECTION. During the study period, the University of Ottawa Heart Institute provided primary PCI as the dominant reperfusion strategy for STEMI patients presenting in our local health network (10). Since the inception of our regional STEMI system, all data pertaining to primary PCI have been entered in the institution's database. In this context, we identified all patients referred for primary PCI between July 2004 and June 2010 presenting with anterior wall STEMI defined as the following: 1) ischemic chest discomfort of at least 30-min duration and onset within 12 h of presentation; and 2) at least 1 mm (0.1 mV) ST-segment elevation in ≥2 contiguous precordial leads on a standard 12-lead electrocardiogram. We included only patients in whom akinesis or dyskinesis was identified in at least 1 LV apical segment on TTE performed within 7 days of hospitalization. Patients were then divided into 2 groups on the basis of initiation of warfarin therapy during the acute hospitalization. The following were criteria for exclusion: warfarin at the time of admission; atrial fibrillation, deep vein thrombosis, pulmonary embolism, mechanical prosthetic cardiac valve, or LV thrombus; bypass surgery during the same admission; previous intracranial bleeding; in-hospital bleeding or stroke occurring before baseline TTE; and TTE was of suboptimal quality, not performed, or performed >7 days after the admission. We also excluded patients who died within 72 h of admission or in the setting of ongoing cardiogenic shock or anoxic encephalopathy.

STANDARD THERAPY. All patients received 160 mg chewable aspirin, 600 mg oral clopidogrel, and 60 U/kg intravenous unfractionated heparin to a maximal dose of 4,000 U before catheterization. The PCI procedure was performed according to the standard of practice. After the PCI, aspirin 81 mg/day was prescribed to be continued indefinitely and clopidogrel 75 mg/day for up to 1 year. Patients were monitored in the cardiac intensive care unit and, when deemed stable, were transferred to the ward.

All patients were treated with intravenous heparin after the PCI until TTE was performed. The decision to add warfarin was at the discretion of the treating cardiologist. In patients deemed not to require oral anticoagulants, heparin was discontinued immediately after TTE; however, it was continued as bridging therapy in patients started on warfarin. In these patients, warfarin was prescribed for 3 to 6 months and the international normalized ratio (INR) was adjusted between 2.0 and 3.0 as per prevailing guidelines (11,12). Patients were followed in the clinic at the University of Ottawa Heart Institute, and telephone follow-up was performed when a visit was not possible.

ECHOCARDIOGRAPHY. TTE images were acquired using the following systems: the iE33 Echocardiography System (Philips Healthcare, Andover, Massachusetts), the Sono's 5500 (Philips Healthcare) or the Vivid 7 (GE Healthcare, Milwaukee, Wisconsin). Regional LV function was assessed using a 16-segment model as recommended by the American Society of Echocardiography (13). This model consists of 6 segments at the base, 6 at the midventricular level, and 4 at the apex. Each segment was analyzed individually and scored on the basis of its motion and systolic thickening using the following recommended scale: normal or hyperkinesis = 1; hypokinesis = 2; akinesis = 3; dyskinesis = 4; and aneurysmal = 5. At least 1 of the 4 apical segments needed an individual

score of 3, 4, or 5 to meet study inclusion criteria. A LV apical score was generated by summing the scores of the 4 individual apical segments. LV ejection fraction was calculated using Simpson's rule. Contrast agents were used to better visualize LV wall segments and to detect LV thrombus according to American Society of Echocardiography guidelines (14). All images were interpreted by cardiologists with level 3 certification in echocardiography (15). The University of Ottawa Heart Institute echocardiography laboratory is accredited by the Intersocietal Commission for the Accreditation of Echocardiography Laboratories.

ENDPOINTS AND DEFINITIONS. The objective of this study was to determine the benefits of adding warfarin therapy in patients with anterior STEMI initially managed with primary PCI and in whom apical akinesis or dyskinesis was demonstrated on TTE performed within the first week of hospitalization. The primary outcome was a composite of net adverse clinical events (NACE) consisting of all-cause mortality, stroke, reinfarction, and major bleeding within 180 days of the index TTE. A stroke was defined as a new neurological deficit of >24-h duration and was classified as hemorrhagic or nonhemorrhagic on the basis of computed tomography or magnetic resonance imaging of the head. Reinfarction was defined as recurrent chest pain associated with re-elevation of the ST segments in association with re-elevation of cardiac enzymes (twice the upper limit of the normal range) or angiographic documentation of reocclusion of the infarct-related artery. Major bleeding was defined as the need for at least 1 blood transfusion or intracranial bleeding confirmed by imaging. In patients prescribed warfarin, bleeding was not included as an event if the event occurred more than 7 days after stopping this therapy. A composite of major adverse cardiovascular events consisting of death, myocardial infarction, and stroke was a secondary endpoint. We also evaluated for definite or probable stent thrombosis as defined by the Academic Research Consortium criteria (16). The study was approved by the institutional review board of the University of Ottawa Heart Institute.

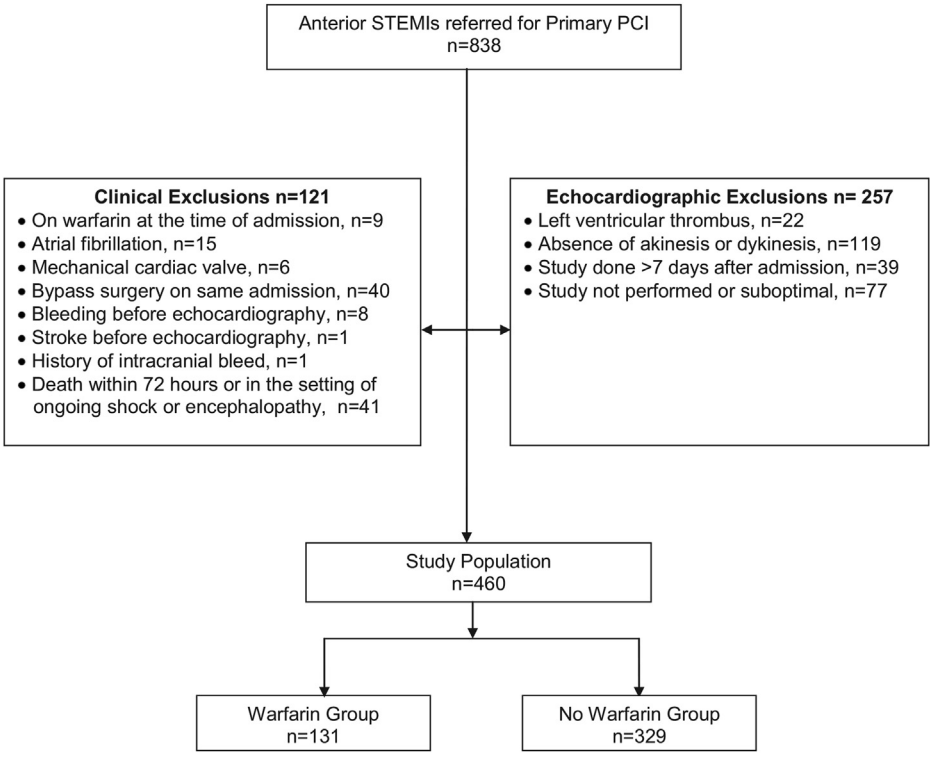

FIGURE 1 Flow of Patients in the Study

Between July 2004 and June 2010, a total of 838 consecutive patients presenting with anterior STEMI were screened. As shown in the figure, 460 patients qualified for the study: 131 were discharged on warfarin therapy and 329 were discharged without warfarin therapy. PCI = percutaneous coronary intervention; STEMI = ST-segment elevation myocardial infarction.

STATISTICAL ANALYSIS. Categorical variables are presented as frequencies (percentages) and were compared by the Fisher exact test or the chi-square test, as appropriate. Normally distributed continuous variables are shown as mean ± SD and were compared with the Student *t* test. Nonnormally distributed variables are shown as median (interquartile range) and were analyzed with the Mann-Whitney *U* test. The LV ejection fraction and the apical score were compared between baseline and follow-up TTE studies using a paired *t* test. A propensity score was generated using the baseline variables, and the impact of warfarin therapy on NACE at 180 days was assessed on the basis of a propensity score analysis using inverse probability weighting in a logistic regression model. In addition, a multivariable analysis using a logistic regression model was performed to determine the independent effect of adding warfarin therapy on NACE, controlling for differences in baseline variables with $p < 0.10$ by univariable analysis. A 2-sided p value ≤0.05 was considered statistically significant. Analyses were conducted using SAS version 9.13 (SAS Institute, Cary, North Carolina).

TABLE 1 Baseline Characteristics of Patients

Characteristic	Warfarin (n = 131)	No Warfarin (n = 329)	p Value
Age, yrs	61.5 ± 14.1	60.6 ± 14.2	0.53
Male	96 (73.3)	248 (75.4)	0.64
Hypertension	54 (42.5)	129 (40.1)	0.67
Diabetes mellitus	22 (17.0)	43 (13.2)	0.30
Current smoker	51 (39.2)	137 (42.3)	0.60
History of hyperlipidemia	43 (34.4)	120 (37.7)	0.58
Previous myocardial infarction	10 (7.8)	32 (9.9)	0.59
Previous stroke	8 (6.2)	13 (4.0)	0.33
Previous angioplasty	11 (8.5)	20 (6.2)	0.41
Previous bypass surgery	2 (1.5)	1 (0.3)	0.20
Heart rate, beats/min	83.9 ± 18.7	81.3 ± 18.8	0.13
Systolic blood pressure, mm Hg	136.2 ± 27.7	138.4 ± 28.4	0.46
Diastolic blood pressure, mm Hg	84.2 ± 16.6	83.1 ± 17.7	0.63
Killip class			0.56
I	104 (79.4)	279 (84.8)	
II	19 (14.5)	38 (11.6)	
III	3 (2.3)	5 (1.5)	
IV	5 (3.8)	7 (2.1)	
Body mass index, kg/m^2	27.9 ± 5.7	27.4 ± 5.0	0.35
Creatinine clearance, ml/min	84.2 ± 35.8	89.7 ± 37.7	0.14
Baseline hemoglobin, g/l	147.4 ± 17.1	144.0 ± 17.5	0.06
Time to TTE, days	2 (1-2)	2 (1-3)	0.006
Left ventricular ejection fraction, %	39.0 ± 8.5	44.7 ± 8.2	<0.0001
Left ventricular apical score	12.9 ± 2.2	11.1 ± 1.9	<0.0001
Discharge medications			
Aspirin	131 (100)	325 (98.8)	0.58
Clopidogrel	130 (99.2)	325 (98.9)	1.00
Dual-antiplatelet therapy	130 (99.2)	320 (97.6)	0.46
Angiotensin-converting enzyme inhibitor	118 (90.1)	283 (86.0)	0.28
Angiotensin receptor blocker	4 (3.1)	15 (4.6)	0.61
Beta-blocker	104 (93.7)	295 (96.1)	0.30
Statin	126 (96.2)	323 (98.2)	0.31

Values are mean ± SD, n (%), or median (interquartile range).
TTE = transthoracic echocardiography.

RESULTS

PATIENTS. We screened 838 consecutive patients presenting with anterior STEMI between July 2004 and June 2010. TTE was performed in 751 of these patients, and LV thrombus was reported in 22 patients (2.9%). As shown in Figure 1, of 460 patients who qualified for the study, 131 patients were discharged on warfarin therapy and 329 were discharged without warfarin therapy. Baseline characteristics of the patients are shown in Table 1. The 2 groups were relatively well matched except for the following: in patients treated with warfarin therapy, hemoglobin was higher (147.4 ± 17.1 g/l vs. 144.0 ± 17.5 g/l); the LV apical score was higher (12.9 ± 2.2 vs. 11.1 ± 1.9, $p < 0.0001$); and the LV ejection fraction was lower (39.0 ± 8.5 vs. 44.7 ± 8.2, $p < 0.0001$). At discharge, DAPT was prescribed for 99.2% of the patients in the warfarin group (i.e., triple therapy) and for 97.6% of the patients in the no warfarin group ($p = 0.46$). The distribution of patient's apical scores in the 2 groups is depicted in Figure 2.

PROCEDURE RESULTS. All patients underwent cardiac catheterization. As shown in Table 2, more patients in the warfarin group underwent primary PCI (100% vs. 95.4%, $p = 0.01$), and bivalirudin was used less frequently in this group (22.9% vs. 34.3%, $p = 0.02$). Compared with patients not prescribed warfarin therapy, the proportion of patients with Thrombolysis In Myocardial Infarction (TIMI) flow grade 3 at baseline in the warfarin group was lower (22.6% vs. 13.0%, $p = 0.02$); however, there was no difference in the proportion of patients with TIMI flow grade 3 after the procedure (92.3% vs. 88.6%, $p = 0.20$).

FOLLOW-UP ECHOCARDIOGRAPHY. During the follow-up period, TTE was repeated in 190 patients: 71 patients in the warfarin group and 119 in the no warfarin group. LV thrombus was not observed in any patient. In the warfarin group, the LV ejection fraction increased from 38.3 ± 8.1 at baseline to 42.0 ± 11.4 at follow-up ($p = 0.004$), and the apical score decreased from 12.6 ± 2.0 to 11.3 ± 4.2 ($p = 0.02$). Similarly, in the no warfarin group, the LV ejection fraction increased from 43.6 ± 8.5 to 47.8 ± 11.0 ($p < 0.0001$), and the apical score decreased from 11.3 ± 1.8 to 9.1 ± 3.9 ($p < 0.0001$). Apical akinesis or dyskinesis was no longer present in 21% of patients

in the warfarin group and in 41% of patients in the no warfarin group.

CLINICAL RESULTS. Clinical events are shown in Table 3. Complete follow-up was available in 99.0% of the patients. Compared with patients who were not prescribed warfarin, patients who were prescribed warfarin had a higher rate of NACE at 180 days (14.7% vs. 4.6%, p = 0.001). The rate of death was higher in patients prescribed warfarin (5.4% vs. 1.5%, p = 0.04, and the rate of stroke was also higher (3.1% vs. 0.3%, p = 0.02). Two patients in the warfarin group (1.5%) versus none in the no warfarin group experienced a hemorrhagic stroke (p = 0.08). There was no difference in the rates of reinfarction between the 2 groups. The need for blood transfusion was higher in the warfarin group (7.8% vs. 1.8%, p = 0.004), as was major bleeding (blood transfusion or hemorrhagic stroke) (8.5% vs. 1.8%, p < 0.0001). Bleeding at the access site used for cardiac catheterization occurred in 4 patients (3.1%) in the warfarin group and in none of the patients in the no warfarin group (p = 0.006). One patient in the warfarin group received a blood transfusion more than 1 week after stopping warfarin; however, by protocol, this was not included in the analysis as a bleeding event. The median length of stay during the initial hospitalization was longer in the warfarin group (8 days vs. 5 days, p < 0.0001). The number of readmissions was also higher (19.4% vs. 9.2%, p = 0.004).

The impact of warfarin therapy on NACE was assessed by propensity score analysis. The odds ratio (OR) of NACE was noted to be higher in the group of patients treated with warfarin (OR: 4.01, 95% confidence interval [CI]: 2.15 to 7.50, p < 0.0001). The C-statistic was 0.67. The impact of warfarin therapy was also assessed in a multivariable logistic regression analysis. The following variables with p < 0.10 were entered in the model: patient group (warfarin vs. no warfarin), admission hemoglobin level, femoral access, PCI done at initial angiography, bivalirudin used during the PCI, initial TIMI flow grade 3, time from admission to TTE, baseline LV apical score, baseline LV ejection fraction, and shock during the initial hospitalization. In patients prescribed warfarin, the OR of NACE remained significantly higher compared with patients who were not prescribed warfarin (OR: 3.13, 95% CI: 1.34 to 7.22, p = 0.007). The C-statistic was 0.72.

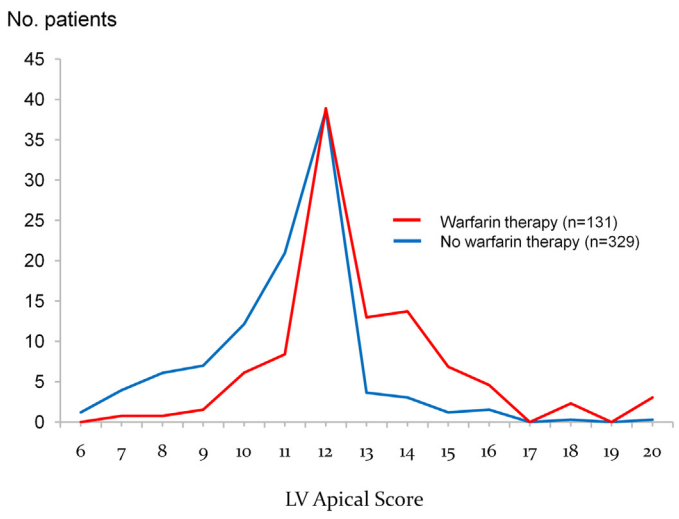

FIGURE 2 Distribution of LV Apical Scores in the 2 Groups

An apical score was generated by summing the scores of the 4 individual apical segments reported on the transthoracic echocardiography: the range for an apical score was 6 to 20. The figure highlights the extent of overlap between the 2 groups. LV = left ventricular.

DISCUSSION

In this study, the addition of warfarin to prevent thromboembolic complications in patients presenting with anterior STEMI treated with primary PCI was associated with more adverse clinical events compared with patients who were managed without warfarin therapy. Our results suggest that in the absence of LV thrombus, the addition of warfarin is not indicated for the management of patients with apical akinesis or dyskinesis on TTE.

Compared with aspirin alone, clopidogrel added to aspirin reduces cardiovascular events in patients with acute coronary syndrome (17). Likewise, DAPT consisting of aspirin and a thienopyridine reduces cardiac events after coronary stent placement compared with aspirin alone or aspirin with oral anticoagulants (1–4). Hence, DAPT has become the standard of care in patients presenting with an acute coronary syndrome and in patients treated with coronary stenting.

Triple therapy consists of oral anticoagulant therapy plus DAPT (9). In some patients with acute coronary syndrome, warfarin therapy is also needed for protection against thromboembolic disease because of other coexisting medical conditions such as atrial fibrillation, prosthetic mechanical valves, venous thromboembolic disease, and hypercoagulable disorders. The current American College of Cardiology/American Heart Association STEMI guidelines indicate that anticoagulant therapy with a vitamin K antagonist is reasonable for patients with STEMI and asymptomatic LV mural thrombi and may be considered for patients with anterior apical akinesis or

TABLE 2 Procedural Results

Variable	Warfarin (n = 131)	No Warfarin (n = 329)	p Value
Catheterization performed	131 (100.0)	329 (100.0)	
Femoral access	111 (84.7)	299 (90.9)	0.07
PCI performed	131 (100.0)	314 (95.4)	0.01
Stenting performed	127 (96.9)	310 (94.2)	0.34
Stents per patient	1.5 ± 0.8	1.4 ± 0.8	0.21
Drug-eluting stent implanted	39 (30.7)	107 (34.5)	0.50
Glycoprotein IIb/IIIa inhibitor use	56 (41.8)	121 (36.8)	0.24
Bivalirudin use	30 (22.9)	113 (34.3)	0.02
Aspiration catheter use	42 (34.1)	97 (32.1)	0.73
Multivessel disease	52 (39.7)	141 (42.9)	0.60
Coronary flow at baseline			0.03
TIMI grade			
0	90 (68.7)	176 (53.8)	
1	11 (8.4)	31 (9.5)	
2	13 (9.9)	46 (14.1)	
3	17 (13.0)	74 (22.6)	
Coronary flow after procedure			0.07
TIMI grade			
0	0 (0.0)	4 (1.2)	
1	1 (0.8)	5 (1.5)	
2	14 (10.7)	16 (4.9)	
3	116 (88.6)	301 (92.3)	
Stenosis, % of luminal diameter			
Before procedure	97.8 ± 8.6	97.2 ± 7.1	0.46
After procedure	2.0 ± 11.0	0.7 ± 6.4	0.19
Door-to-balloon time, min	98 (72-130)	96 (70-134)	0.48
Onset-to-balloon time, min	211 (158-360)	205 (143-347)	0.32
Therapeutic hypothermia use	2 (1.5)	4 (1.2)	1.00
Intra-aortic balloon counter pulsation use	5 (3.8)	7 (2.1)	0.33

Values are n (%), mean ± SD, or median (interquartile range).
PCI = percutaneous coronary intervention.

TABLE 3 Clinical Outcomes

Outcomes	Warfarin (n = 131)	No Warfarin (n = 329)	p Value
In-hospital			
Death	0 (0.0)	0 (0.0)	–
Reinfarction	1 (0.8)	0 (0.0)	0.29
Stroke	1 (0.8)	1 (0.3)	0.49
Hemorrhagic	0 (0)	0 (0)	
Blood transfusion	4 (3.1)	0 (0.0)	0.006
Major bleeding	4 (3.1)	0 (0.0)	0.006
Death, reinfarction or stroke	2 (1.5)	1 (0.3)	0.20
Death, reinfarction, stroke or major bleeding	6 (4.6)	1 (0.3)	0.003
Stent thrombosis	1 (0.8)	0 (0.0)	0.29
Cardiogenic shock	14 (10.7)	10 (3.0)	0.002
Length of stay, days	8 (7-11)	5 (4-7)	<0.001
Cumulative events at 180 days			
Death	7 (5.4)	5 (1.5)	0.04
Reinfarction	2 (1.6)	5 (1.5)	1.00
Stroke	4 (3.1)	1 (0.3)	0.02
Hemorrhagic	2 (1.5)	0 (0)	0.08
Blood transfusion	10 (7.8)	6 (1.8)	0.004
Major bleeding	11 (8.5)	6 (1.8)	<0.0001
Death, reinfarction or stroke	12 (9.3)	9 (2.8)	0.005
Primary outcome: death, reinfarction, stroke, or major bleeding	19/129 (14.7)	15/327 (4.6)	0.001
Stent thrombosis	1/129 (0.8)	3/327 (0.9)	1.000
Hospital readmission	25 (19.4)	30 (9.2)	0.004

Values are n (%), median (interquartile range), or n/N (%).

dyskinesis (9). To assess the benefits associated with the latter indication, we excluded patients with LV thrombus as well as patients with a coexisting condition needing warfarin therapy.

The risk of major bleeding with triple therapy has been reported to be 2 to 5 times higher compared with DAPT alone in patients treated with coronary stenting (5-8). However, outcome data on the use of triple therapy in patients treated with primary PCI remain limited. In our study, 99.2% of the patients in the warfarin group were discharged on DAPT (i.e., received triple therapy), whereas 97.6% of the patients in the no warfarin group were discharged on DAPT. In a recent analysis from the HORIZONS-AMI (Harmonizing Outcomes With Revascularization and Stents in Acute Myocardial Infarction) trial, patients with STEMI treated with triple therapy versus DAPT had comparable ischemic outcomes but significantly increased rates of major bleeding at both early and long-term follow-up (18). Our study differs in that we included only patients with apical akinesis or dyskinesis documented by TTE, and we excluded patients with LV thrombus and patients with other indications for oral anticoagulation. That said, major bleeding was also higher in patients managed with warfarin therapy in our study. Perhaps more concerning, major adverse cardiovascular events (i.e., death, reinfarction, stroke), were more frequent in the warfarin group, including a higher rate of strokes with a trend toward more hemorrhagic strokes in this group.

Most studies comparing outcomes between triple therapy and DAPT typically included patients with different indications for warfarin therapy, the most frequent being atrial fibrillation. In 1 retrospective study involving 426 patients with atrial fibrillation undergoing coronary stenting, nonanticoagulation with warfarin was an independent predictor of increased mortality (19). A recent meta-analysis of nonrandomized studies suggested that triple therapy is more efficacious than DAPT in the prevention of major adverse cardiovascular events including all-cause mortality (20). However, in this meta-analysis, warfarin therapy was prescribed mostly for atrial

fibrillation. Therefore, these results were not completely unexpected given that a large randomized trial previously demonstrated the superior benefits of warfarin therapy for the prevention of vascular events compared with aspirin plus clopidogrel in patients with atrial fibrillation (21). Because we excluded patients with atrial fibrillation and other medical conditions necessitating oral anticoagulant therapy, patient selection may explain why warfarin therapy was not beneficial in our STEMI patients.

Of note, we excluded 22 patients with LV thrombus (2.9%) from this study because most physicians would have been compelled to use anticoagulants in these patients. This incidence is lower than the 6.2% to 23.5% reported in previous studies on patients with anterior STEMI managed with different reperfusion strategies (22,23) and may be related to the extent of rapid, complete, and sustained reperfusion associated with primary PCI in our citywide program (10).

STUDY LIMITATIONS. First, because it was not a randomized trial, it is possible that unappreciated or immeasurable confounding variables could have altered the results. Our study was conducted with data from real-world patients. For this reason, we attempted to correct imbalances between groups by multivariable and propensity score analysis. Because the rate of stroke in our patients managed without warfarin was extremely low, a randomized trial would require a very large sample size to show the benefit of reducing the rate of this complication by the addition of warfarin therapy. As such, our results may be the most definitive evidence to guide clinicians. Furthermore, bleeding events in our patients treated with warfarin are in keeping with other reports on triple therapy. There is mounting evidence that bleeding complications after PCI are associated with mortality (24), and several studies found a link between blood transfusion and excess mortality (24–27). Second, we did not report the INR measurements at the time of the events. Current guidelines recommend that the INR be tightly controlled when warfarin therapy is added to DAPT (9). One study found that INR values were higher in patients on triple therapy who experienced a bleeding complication (8). However, a recent study concluded that triple therapy compared with DAPT predisposes patients to an increased risk of major bleeding complications regardless of the time spent in the therapeutic anticoagulation range (28).

CONCLUSIONS

Our results do not support the addition of warfarin therapy after primary PCI in patients with apical akinesis or dyskinesis. Review of the current guidelines may be warranted.

REPRINT REQUESTS AND CORRESPONDENCE: Dr. Michel R. Le May, Ottawa Heart Institute, 40 Ruskin Street, Ottawa, Ontario K1Y 4W7, Canada. E-mail: mlemay@ottawaheart.ca.

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